Attorney Docket No.: 62611.000167
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:	)	
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F. C. Thomas ALLNUTT, et al.	)	Examiner: Changhwa J. CHEU
	)	
Serial No.: 09/937,477	)	Group Art Unit: 1641
	)	
Filed: January 23, 2002	)	

For: SPECIFIC BINDING ASSAY FOR DOCOSAHEXAENOIC ACID

RESPONSE TO NON-FINAL OFFICE ACTION

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Response is filed in reply to the U.S. Patent and Trademark Office (USPTO) non-final Office Action mailed August 20, 2004 in the above-captioned application (the Application). The Office Action had been mailed to the Attorney of Record's previous firm's address even though a Change of Correspondence Address had been filed on April 4, 2003. Applicants discovered that an Office Action had been mailed, though one had not been received, when Applicants' representative checked the status of the application on the Patent Application Information Retrieval (PAIR) system on December 30, 2004. Therefore, the time for response should be calculated from no earlier than December 30, 2004 when the Applicants were first aware of the Office Action.

Applicants note that a request to reissue the Office Action was filed on January 6, 2005. Therefore, Applicants believe no extension of time fee is due. However, should it be determined by the USPTO that any fees are necessary for reconsideration of this application, including an extension of time fee, the Commissioner is authorized to charge such necessary fees to the undersigned's Deposit Account No. 50-0206.

I. Restriction Requirement

The Examiner stated that the common technical feature is a protein that specifically binds docosahexaenoic acid (DHA), which is not novel, and thus, the invention lacks unity of inventive concept under 35 U.S.C. §§ 121 and 372. This restriction is respectfully traversed.

The common technical feature of the claims is an assay based on detection of the DHA-protein complex, not the protein that specifically binds DHA. Because assays incorporating the detection of the DHA-protein complex are novel, the invention does, in fact, possess unity of inventive concept. Therefore, Applicants respectfully request that the restriction be withdrawn. However, in the event that the restriction is maintained, Applicants elect with traverse Group I, claims 1-13, drawn to a method for detecting the presence or amount of DHA in a sample.

II. Claim Rejections

Claims 12 and 13 stand rejected as allegedly failing to comply with the enablement and written description requirements under 35 U.S.C. § 112, first paragraph. Claims 9 and 12 stand rejected as allegedly being indefinite under 35 U.S.C. § 112, second paragraph. Claims 1, 2 and 4-9 stand rejected as allegedly being anticipated by Xu *et al.*, *J. Biol. Chem*, 271(40):24711-9 (1996) (Xu) under 35 U.S.C. § 102(b). Finally, claim 3 stands rejected as allegedly being obvious over Xu in view of U.S. Patent No. 6,326,159 issued to Ullman *et al.* (Ullman), and claims 10 and 11 stand rejected as allegedly being obvious over Xu under 35 U.S.C. § 103(a).

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 12 and 13 for allegedly failing to describe the claimed subject matter in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner further rejected claims 12 and 13 for allegedly failing to describe the claimed subject matter in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention at the time the application was filed. These rejections are respectfully traversed.

With regard to the enablement rejection, the Examiner asserts that the specification does not state what kind of agent(s) can be used to release DHA from complex lipids nor does it provide a working example of the hydrolysis. The Examiner cites Example 4 for the proposition

that Applicants discuss the use of detergents or lipid micelles to "take up" the released fatty acid but that the function of detergents or lipid micelles is not hydrolysis. Office Action, page 4.

Applicants respectfully submit that claims 12 and 13 are enabled. The specification states, "[C]omplex lipid materials may be saponified to release DHA as a free fatty acid to facilitate the assay. Methods of saponification are within the skill of the ordinary worker in the art." Page 9, lines 24-26. It also provides that treating the sample with a base, such as 8 M KOH in methanol, would accomplish saponification (i.e. non-enzymatic hydrolysis) to release DHA as a free fatty acid. This procedure is further described in Example 1 on page 18. Example 4, which was referenced by the Examiner, states that the sample was prepared as described in Example 1. Therefore, the DHA had already been released from the complex lipids prior to the addition of the detergent or lipid micelles.

The specification also provides an example of enzymatic hydrolysis. The specification states:

> In yet another embodiment, the DHA-containing sample is treated with PUFA-specific lipases which release DHA as a free fatty acid. Such treatment is done in an aqueous environment, then the assay is carried out directly in the aqueous environment. Detergents that do not disrupt the BLBP but do more easily mobilize the fatty acid or lipid could be used to homogenize the sample to provide more complete presentation of the fatty acid to its specific binding partner FABP.

Page 10, lines 4-9.

The Examiner further stated that the skilled artisan cannot envision the detailed hydrolyzing agent(s) specific for DHA and therefore, the written description requirement had not been satisfied with regard to claims 12 and 13. Applicants respectfully disagree. As explained above, the specification describes, *inter alia*, saponification as a method for non-enzymatic hydrolysis and the use of lipases for enzymatic hydrolysis to release DHA from complex lipids as a free fatty acid. Saponification and transesterification have been used by analytical chemists to release free fatty acids and fatty acid methyl esters from complex lipid esters of fatty acids for over a century. Thus, one skilled in the art could recognize that Applicants invented what is claimed.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 9 and 12 for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection.

First, the Examiner asserted that "immobilized" as recited in claim 9 is vague and indefinite because it was not clear as to where and how the protein is immobilized. Applicants respectfully submit that "immobilized" is described in the specification at page 13, lines 15-23:

> The DHA-binding protein may be immobilized to a manufactured solid support, such as a microtitration dish, microparticle, polymeric bead, polymer matrix, polymer, synthetic membrane, liposome, glass, etc. . . . The attachment may be covalent or noncovalent, specific or non-specific. The method of attachment may be optimized to achieve a preferred orientation of the protein relative to the solid surface. For some applications, it may be desirable that the protein or lipid binding partner be attached in an ordered array, such as in a grid or other pattern.

Second, the Examiner asserted that "complex lipids" in claim 12 is vague and indefinite because it is not clear as to whether this complex is the same as the "DHA-protein complex" as recited in claim 1. Applicants respectfully submit that "complex lipids" is described in the specification at page 9, lines 23-29, which states in part, "Complex lipid materials *containing* DHA moieties which bind the DHA-binding protein may be assayed directly" (emphasis added). Moreover, "complex lipids" are described in the section regarding obtaining and preparing a sample whereas the DHA-protein complex is what is detected in the sample.

Rejections under 35 U.S.C. § 102(b)

The Examiner rejected claims 1, 2 and 4-9 as allegedly being anticipated by Xu. Applicants respectfully traverse this rejection.

The Examiner asserts that Xu discloses a method of detecting "DHA by using its recognizing protein, i.e. brain lipid-binding protein (BLBP)." Office Action, page 6. The Examiner then describes an experiment to measure the binding between the fatty acid and BLBP. As pointed out by the Examiner, Xu describes a binding affinity study, not a detection assay. Xu was not detecting the presence of DHA because it was known that DHA was present and in what amount. Instead, Xu was determining whether and to what degree (i.e. the binding parameters) DHA would bind to BLBP.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The binding affinity experiment disclosed in Xu utilizes purified samples of the protein and known amounts of fatty acids. Conversely, Applicants' invention detects DHA in a sample that may be biological or food (see page 8, lines 25-29). Biological and food samples contain various components that would interfere with a binding affinity experiment for a particular protein. Therefore, Xu does not anticipate Applicants' invention because every element of the claimed invention is not disclosed in Xu.

Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claim 3 as allegedly being unpatentable over Xu in view of Ullman. The Examiner also rejected claims 10 and 11 as allegedly being unpatentable over Xu. Applicants respectfully traverse these rejections.

With regard to claim 3, the Examiner again asserts that Xu discloses a method for detecting DHA but that Xu is silent in using a protein to detect the DHA-BLBP complex. The Examiner, however, asserts that Ullman discloses the use of a second antibody specific for the immune complex to detect binding. Thus, it would have been obvious to one skilled in the art at the time of Applicants' invention to combine the method used in Xu with the immune complex-specific antibody in Ullman.

Applicants respectfully disagree with the Examiner's assertion. In order to establish a prima facie case of obviousness, "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings." M.P.E.P. § 2142. There is no such suggestion or motivation to combine the references in either reference. Furthermore, one of ordinary skill in the art would not be motivated to combine the references because Xu discloses an experimental determination of binding affinity, not a detection assay, whereas Ullman discloses an immunoassay wherein binding affinity is already known. It is Applicants' disclosed detection assay that makes the combination obvious, but Applicants' disclosure cannot be used to provide motivation to combine the references.